UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/566,502 | 02/06/2006 | Katashi Nakashima | 20060018A | 7557 |

513 7590 02/19/2010

WENDEROTH, LIND & PONACK, L.L.P.
1030 15th Street, N.W.,
Suite 400 East
Washington, DC 20005-1503

| EXAMINER | |
|---|---|
| GHALI, ISIS A D | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1611 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 02/19/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ddalecki@wenderoth.com
eoa@wenderoth.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/566,502 | NAKASHIMA ET AL. | |
| | Examiner | Art Unit | |
| | Isis A. Ghali | 1611 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1,4-9,11 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-9,11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The prosecution of this application has been transferred from examiner Christopher Pochas to examiner Isis Ghali.

Claims 2, 3, 10, 12, and 14-16 have been canceled.

The examiner noticed that claim 1 was improperly identified as "original".

Claims 1, 4-9, 11 and 13 are pending and included in the prosecution.

### *Double Patenting*

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1, 4-9, 11 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 11/815,499. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter claimed in the instant application is fully disclosed in the referenced copending applications and would be covered by any patent granted on the copending applications since the referenced copending applications and the instant application are claiming common subject matter as follows: transdermal preparation containing 4-(2-methyl-l-imidazoolyl)-2,2-diphenylbutylamide. The present claims and the co-pending claims are obvious over each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 4-9, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the article by Miyachi et al. ("Synthesis and Antimuscarinic Activity of a Series of 4-(1-Imidazolyl)-2,2-diphenylbutyramides: Discovery of Potent and Subtype-selective Antimuscarinic Agents", IDS filed 01/31/2006), in view of the article by Nitti ("Transdermal Therapy for Overactive Bladder: Present and Future", IDS filed 12/10/2008) and further in view of either Versi et al. (US 2003/0190072, currently listed on PTO 892) or Landau et al. (US 6,846,823, currently listed on PTO 892).

**Applicant Claims**

Claim 1 is directed to a transdermal preparation containing 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide or a medically acceptable salt thereof, and an external preparation base.

**Determination of the Scope and Content of the Prior Art**

**(MPEP §2141.01)**

Miyachi teaches that the inhibitory action of 4-(2-methyl-1-imidazolyl)-2,2-diphenylbutylamide (KRP-197) on bladder contractions is 15-19 times more potent than oxybutynin and with a similar duration of action (p 1157, col.1, ¶ 2). KRP-197 is fivefold more selective for bladder than oxybutynin (p 1157, col.2, ¶ 2),

**Ascertainment of the Difference Between Scope the Prior Art and the Claims**

**(MPEP §2141.012)**

Miyachi however is silent regarding dosage forms and routes of administration of KRP-197.

Nitti teaches that transdermal delivery of certain pharmacologic agents that treat overactive bladder offers distinct advantages including the ability to bypass the gastrointestinal environment, fewer side effects, and increased bioavailability (page 531). Further, administration of anticholinergic drugs transdermally demonstrated a significant reduction in the anticholinergic side effects that often lead to frustration and

treatment discontinuation (page 533, col.3, ¶ 1). Nitti concludes that the studies that compare oral with transdermal overactive bladder medications with respect to patient satisfaction and preference may help promote more widespread use of transdermal drug delivery as first line therapy for overactive bladder (page 536, col.1 and 2).

Versi teaches treating of varieties of incontinence-related conditions using antimuscarinic agents including KRP-197 (abstract; paragraphs 0010, 0016; table 2; claim 27). The active agents can be administered by means of transdermal patch using conventional technology in order to reduce side effects and obtain improved subject compliance (paragraph 0070). Transdermal patches may contain adhesive reservoir containing the drug dissolved and/or dispersed in the adhesive (paragraph 0080). The teaching of Versi of dissolved and/or dispersed drug in the reservoir meets the limitation of claim 9 that drug is dissolved and non-dissolved.

Landau teaches treating at least one symptoms of lower urinary tract disorder including urinary frequency, urgency, incontinence, nocturia and enuresis using composition comprising antimuscarinic including KRP-197 (abstract; col.18, lines 38-43; col.20, line 18). The composition can be transdermal composition delivered from patch that provides controlled release of the drug through the skin for long period from one application (col.38, lines 40-42, 50-55). Transdermal patch comprises laminate structure comprising backing layer, release liner, and reservoir containing the drugs and permeation enhancer (col.45, lines 5-43).

Adhesive taught by Versi and Landau and permeation enhancer taught by Landau read on the claimed external preparation means because according to

applicants' disclosure on page 15, lines 1-7, "external preparation base" can be amphipathic solubilizing agent, a suspension base, a softener, an emulsifier, a buffer, a transdermal permeability enhancer, a tackifier, a tackiness enhancer, an adhesive, a skin irritancy mitigator, and an additive.

**Finding of Prima Facie Obviousness Rational and Motivation**

**(MPEP §2142-2143)**

At the time of the invention it was known that KRP-197 is antimuscarinic drug that is more potent than other antimuscarinic drugs known as this time such as oxybutynin as taught by Miyachi. At the time of the invention Nitti preferred transdermal delivery of drugs that treat overactive bladder and suggested more widespread use of transdermal drug delivery as first line therapy for overactive bladder. It was further known at the time of the invention that KRP-197 can be delivered in transdermal devices as taught by both of Versi and Landau.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention treat overactive bladder using KRP-197 as taught by Miyachi and deliver the drug transdermally as taught by Nitti, Versi and Landau. One would have been motivated to do so because Nitti teaches that transdermal delivery of pharmacologic agents that treat overactive bladder offers distinct advantages including the ability to bypass the gastrointestinal environment, fewer side effects, and increased bioavailability, and further, administration of anticholinergic drugs transdermally demonstrated a significant reduction in the anticholinergic side effects that often lead to

frustration and treatment discontinuation and suggests more widespread use of transdermal drug delivery as first line therapy for overactive bladder. One would further be motivated to deliver KRP-197 utilizing transdermal device because both of Versi and Landau teaches that KRP-197 can be delivered from transdermal devices that provides reduced side effects, improved patient compliance and controlled release of the drug. One would reasonably expect formulating transdermal device comprising KRP-197 that delivers the drug in a controlled manner to treat urinary bladder disorders effectively with minimal undesired side effects and improved patient compliance.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

7. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Miyachi et al. in view Nitti and either Versi et al. or Landau et al. as applied to claims 1, 4-9 and 11, and further in view of Luo et al. (US 6,586,000, currently listed on PTO 892).

**Applicant Claims**

Claim 13 is further recite the structure of the transdermal device comprising a reservoir, comprising a mixture of 4-(2-methyl-l-imidazolyl)-2,2-diphenylbutylamide and a single or combination of the external preparation bases; and a structural body

comprising a membrane for controlling drug permeation, an adhesive layer, a support, and a peelable liner.

**Determination of the Scope and Content of the Prior Art**

**(MPEP §2141.01)**

The combined teaching of Miyachi, Nitti, and either one of Versi or Landau are discussed above. The combination of the references teaches transdermal device comprising KRP-197, and Landau further teaches transdermal device comprising reservoir, backing layer and peelable release liner.

**Ascertainment of the Difference Between Scope the Prior Art and the Claims**

**(MPEP §2141.012)**

The references however, do not teach the structure of the transdermal device to comprise a membrane to control the release of the drug and the adhesive layer as claimed by claim 13.

Luo teaches transdermal device comprising reservoir containing active agent, adhesive, and further permeation enhancer. The device comprises backing layer, release liner, skin contact adhesive and rate controlling membrane to control the rate at which the drug permeates out of the device (col.4, lines 17-33; col.25, lines 41-43; col.26, lines 10-15). The skin contact adhesive maintains the device in transmitting relationship to the body surface (col.4, lines 27-30).

**Finding of Prima Facie Obviousness Rational and Motivation**

**(MPEP §2142-2143)**

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention treat overactive bladder using KRP-197 delivered from transdermal device comprising reservoir containing the drug, backing layer and peelable release liner as taught by the combination of Miyachi, Nitti, Versi and Landau and further add a rate controlling membrane and skin contact adhesive to the device as taught by Luo. One would have been motivated to do so because Luo teaches the rate controlling membrane controls the rate at which the drug permeates out of the device and the skin contact adhesive layer maintains the device in transmitting relationship to the body surface. One would reasonably expect formulating transdermal device comprising KRP-197 in an adhesive reservoir having backing layer and peelable release liner and further has rate controlling membrane and skin contact adhesive layer wherein the device deliver the drug to the skin in a controlled manner while being secured to the skin of the user.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis A. Ghali whose telephone number is (571) 272-

0595. The examiner can normally be reached on Monday-Thursday, 6:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

IG